REMARKS

Following entry of the foregoing amendments, claims 4 to 7, 34, 37, 38, 46, 49 to 51, 53 to 63, 65, 72, 74 to 78, 94 to 96, 104, and 105 will be pending in this patent application. Claims 34, 50, and 51 have been amended, herein. No claims have been canceled, and no new claims have been added. Support for the amendments is found throughout the specification as originally filed, including, for example, paragraph 207 and the experimental examples. The amendments thus do not introduce new matter into the application.

Applicants respectfully request reconsideration of the rejections of record in view of the foregoing amendments and the following remarks.

Alleged Obviousness

Claims 4 to 7, 34, 37, 38, 46, 49 to 51, 53 to 63, 65, 72, 74 to 78, 94 to 96, 104, and 105 have been rejected under 35 U.S.C. § 103(a) as allegedly obvious over Elbashir *et al.*, *EMBO Journal*, 2001, 20, 6877-6888 ("the Elbashir article"); published U.S. patent application number U.S. 2003/0143732 ("the Fosnaugh application"); and published U.S. patent application number U.S. 2003/0206887 ("the Morrissey application") in view of the combined teachings of U.S. patent number 6,262,036 ("the Arnold patent"); published U.S. patent application number U.S. 2005/0142535 ("the Damha application"); and U.S. patent number 6,133,246 ("the McKay patent"). Applicants respectfully request reconsideration and withdrawal of the rejection because the presently claimed compositions would not have been obvious to those of ordinary skill in the art at the time of the invention.

To establish *prima facie* obviousness, the Patent Office must demonstrate that the cited prior art reference or combination of references teaches or suggests all the limitations of the claims. *In re Royka*, 490 F.2d 981, 180 U.S.P.Q. 580 (C.C.P.A. 1974); *In re Wilson*, 424 F.2d 1382, 1385, 165 U.S.P.Q. 494, 496 (C.C.P.A. 1970). The Office must also identify "***an apparent reason to combine the known elements in the fashion claimed*** by the patent at issue. To facilitate review, this analysis should be made explicit." *KSR Int'l. Co. v. Teleflex Inc.*, 127 S. Ct. 1727, 1741 (emphasis added)(citing *In re Kahn*, 441, F.3d 977, 988 (Fed. Cir. 2006).

The claims have been amended herein to recite compositions that comprise two chemically synthesized oligomeric compounds in which at least one of the oligomeric compounds comprises ribonucleosides that have 2' substituent groups other than H, OH, or $-OCH_3$ that alternate with β-D-deoxyribonucleosides. As the Office acknowledges, the Elbashir article and the Fosnaugh and Morrissey applications do not teach oligomeric compounds that comprise such a motif of alternating ribonucleosides and β-D-deoxyribonucleosides.[1] Significantly, the Arnold and McKay patents also do not teach such a motif, and the Damha application teaches away from the design and production of oligomeric compounds that comprise this motif.

The Arnold patent describes antisense oligonucleotides that contain alternating modified internucleoside linkages, rather than alternating nucleosides having different 2'substituent groups. The Office asserts that Example 34 of the Arnold patent describes antisense oligonucleotides that comprise alternating 2'-β-D-deoxynucleosides and 2'-modified nucleosides,[2] but Example 34 does not actually describe such oligonucleotides. Rather, example 34 describes a series of oligomers having alternating and mixed internucleoside linkages (methylphosphonate, phosphorothioate and phosphodiester) wherein in some instances the methylphosphonate internucleoside linkages are enriched in the Rp diasteromer relative to the Sp diasteromer. The nucleosides of each oligomer have *identical* 2' groups that are either *all* 2'-H or 2'-O-methyl. The Arnold patent thus does not teach or suggest oligomeric compounds that comprise alternating 2'-substituted and 2'-deoxyribonucleosides

The McKay patent also does not describe such oligomeric compounds, but, rather, describes chimeric oligomeric compounds such as gapmers and wingmers that comprise two or more chemically distinct regions.[3] The patent does not teach that such chimeric oligomeric compounds include 2'-substituted ribonucleosides that alternate with 2'-deoxyribonucleosides.

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[1] Office action dated March 26, 2007, page 9 ("The primary references of Elbashir et al, Fosnaugh et al and Morrissey et al do not teach alternating 2'-β-D-deoxynucleosides with 2'-modified nucleosides.)
[2] *Id.*
[3] Col. 11, lines 32 to 64 and Tables 11, 12, 14, 19, 21, 24, and 26.

Although the Damha application describes oligonucleosides that comprise sugar-modified nucleosides alternating with 2'-deoxynucleosides, the application teaches away from the claimed motif of oligomeric compounds that comprise ribonucleosides having 2' substituent groups other than H, OH, or -OCH_3 that alternate with β-D-deoxyribonucleosides. Specifically, example 3 of the application describes experiments in which various antisense oligonucleotides were evaluated for their ability to elicit degradation of target RNA by *E. coli* RNase HI and human RNase HII. The antisense oligonucleotides used in the experiments contained one to three nucleotide segments of 2'-deoxy-2'-fluoro-D-arabinothymidine nucleotides (FANA) alternating with one to three nucleotide segments of 2'-deoxyribothymidine nucleotides (deoxy T). RNase cleavage efficiency increased as the number of nucleotides in each segment increased, and optimal activity was exhibited by an oligonucleotide (SEQ ID NO:5) that contained alternating trinucleotide segments of FANA and deoxy T. Significantly, the patent indicates that an antisense oligonucleotide containing alternating one nucleotide segments of 2'-O-methyl-D-uridine (2'-O-methyl U) and deoxy T "showed only poor ability to elicit RNase H degradation of target RNA."[4]

The results of these experiments thus teach away from the presently claimed oligomeric compounds. First, the experiments indicate that optimal activity was exhibited by an antisense oligonucleotide containing an alternating motif of nucleosides that differs significantly from that claimed. Specifically, the application teaches that optimal activity was exhibited by an antisense oligonucleotide that contained segments of nucleosides having modified ***arabino*** sugar groups alternating with segments of 2'-β-D-deoxynucleosides, rather than segments of nucleosides having modified ***ribose*** sugar groups alternating with segments of 2'-β-D-deoxynucleosides, as presently claimed. The patent further teaches that optimal activity occurred when the segments of the antisense oligonucleotides were each three nucleotides in length, rather than one nucleotide as presently claimed. Moreover, the patent teaches that antisense oligonucleotides containing alternating one nucleotide segments of 2'-O-methyl U and deoxy T actually exhibited ***poor*** activity. Accordingly, upon review of the Damha application, those skilled in the art would

[4] Paragraph 149.

not have reasonably believed that oligomeric compounds containing the claimed motif of ribonucleosides having 2' substituent groups other than H, OH, or -OCH_3 alternating with β-D-deoxyribonucleosides would have been particularly useful. Those skilled in the art would thus not have been likely to design and produce such oligomeric compounds in light of the teachings of the Damha application.

The Elbashir article, the Fosnaugh and Morrissey applications, and the Arnold and McKay patents thus fail to teach or suggest the claimed compositions that comprise two chemically synthesized oligomeric compounds in which at least one of the oligomeric compounds comprises linked ribonucleosides having 2' substituent groups other than H, OH, or -OCH_3 that alternate with β-D-deoxyribonucleosides. Moreover, the Damha application teaches away from the design and production of such oligomeric compounds. Those skilled in the art thus would have had no apparent reason to make and use oligomeric compounds containing the claimed motif of nucleosides before applicants' invention. Furthermore, as discussed above, without conceding the correctness of the present rejection, claim 34 has been amended herein to recite that the 2'-substituent group of each Q and each Z is other than -OCH_3. The claimed compositions would therefore not have been obvious to those of ordinary skill in the art at the time of the invention, and applicants accordingly, respectfully, request withdrawal of the rejection for alleged obviousness.

Alleged Double Patenting

Claims 4 to 7, 34, 37, 38, 46, 49 to 51, 53 to 63, 65, 72, 74 to 78, 94 to 96, 104, and 105 have been provisionally rejected under the judicially created doctrine of obviousness-type double patenting as allegedly unpatentable over claims 36, 40, 44, 46 to 49, 52 to 64, 74 to 80, 93, 98 to 100, and 104 of copending U.S. patent application number 10/860,265. In addition, claims 4 to 7, 34, 37, 38, 46, 49 to 51, 53 to 63, 65, 72, 74 to 78, 94 to 96, 104, and 105 have been independently provisionally rejected under the judicially created doctrine of obviousness-type double patenting as allegedly unpatentable over claims 1 to 24 of copending U.S. patent application number 11/054,848. Applicants respectfully request that these rejections be deferred

pending the identification of allowable subject matter in the present application, as the rejections can likely be readily resolved, depending upon the subject matter ultimately allowed, through the filing of suitable terminal disclaimers.

Conclusion

Applicants believe that the foregoing constitutes a complete and full response to the official action of record. Accordingly, an early and favorable action is respectfully requested.

Respectfully submitted,

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